KARNATAKA STATE AKKAMAHADEVI WOMEN'S UNIVERSITY, VIJAYAPURA
Jnanashakti Campus, Torvi, Vijayapura

Title of the research work:

"IDENTIFICATION AND VALIDATION OF PLANT BASED BIOACTIVE COMPOUNDS FOR IMMUNOMODULATORY AND ANTI-INFLAMMATORY PROPERTIES"

Pre-synopsis

Submitted towards the partial fulfillment of Ph.D programme in Bioinformatics

Submitted By

Mrs. Tejaswini Hipparagi
Research scholar
Dept. of Bioinformatics, KSAWU Vijayapura

Under the Guidance of

Dr. Babu R L
Assistant Professor
Dept. of Bioinformatics
Karnataka State Akkamahadevi Women's University, Vijayapura

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SYNOPSIS

"Identification and validation of plant based bioactive compounds for Immunomodulatory and anti-inflammatory properties"

1. Introduction

Medicinal plants have played a very important key role in the human body and human health throughout the world for thousands of years. Indeed the vast advances observed in modern medicine in recent decades [1]. Phytochemicals are plant chemicals. A plant material shows an important resource to conflict serious diseases. The traditional medicinal plant and treatment methods are still play essential role to cover the basic health needs in the developing countries. Phytochemicals can be categorized predominantly as major constituents; these bioactive constituents of plants are carbohydrates, lipids, proteins, alkaloids, tannin, flavonoids and phenolic compounds [2].

Many phytochemicals are known for their anti-inflammatory, antitumor, anticancer, anti-diabetic, chemo-preventive, cardio-protective, wound healing, cosmetic and skin protection, antiseptic, antiviral and antibacterial properties. The current trend towards uses of plytochemicals has created an acute need for accurate information, safety, efficacy, and quality of medicinal plant products [3]. The present study focused on three medicinal plants which are known for anti-inflammatory activity. In this connection chosen the plant cassia auriculata linn because this plant having more anti-inflammatory activity.

Cassia auriculata Linn. commonly known as 'Tanner's Cassia' (Ceasalpinaceae) or Avartaki in Ayurveda is an annual or biennial shrub found throughout India in open forests. The leaves are bitter, acrid, thermogenic, astringent, haematinic, constipating and expectorant. Seeds are also bitter, acrid, cooling, astringent, ophthalmic, alexeteric, diuretic and vulnerary. Cassia auriculata linn plant had several medicinal properties. The dried powder of flower bud is used as a tea powder in case of patients and it is also may improve the complexion in women and also considered to be one of the important dye yielding plants in India. It is found in dry zones of southern, western and central India extending up to Rajasthan in North. It is also cultivate in some parts of Punjab, Uttar Pradesh, Haryana and West Bengal, and often planted in gardens for ornament and as hedges [4]. The various parts of the cassia auriculata linn plant has been reported many number of therapeutic activities to manage disease states like rheumatism, asthma, leprosy, gout and diabetes. It is also used as antiulcer, antipyretic, in the treatment of skin infections [5].

Inflammation is the most important part of body's immune. It attempts at response and removing harmful stimuli such as irritants or pathogens, damaged cells to start healing and it also involving immune cells, blood vessels and molecular mediators protective response. Which

conduct to release of pro-inflammatory mediators to the affected tissue causing increased flow of blood to the infection or injury and it results in swelling and redness. It stimulates the nerves and cause pain [6, 7].

Types of inflammation are acute and chronic inflammation. Acute inflammation normally has enhancing within minutes or only hours after tissue injury, and represent by the classical symptoms of swelling, redness, heat, and edema. It is a short term process. And chronic inflammation is more protracted duration and histologically by the presence of lymphocytes and macrophages, emerging in fibrosis and tissue necrosis. The chronic inflammation increases the progress of the regressive diseases such as atherosclerosis, heart disease, Alzheimer, asthma, rheumatoid arthritis [8]. During an inflammatory retaliation, mediators, such as pro-inflammatory cytokines interleukin ((IL-1), IL-6, IL-17, IL-18, IL-23), tumor necrosis factor (TNF-alpha), BAFF, interferon(IFN). Pro-inflammatory mediators are alienated by anti-inflammatory cytokines (IL-4, IL-10, IL-13 and TGF) [9].

In the proposed study photochemical / bioactive compounds of selected plant is screened for anti-inflammatory activity using *Insilico* tools. Bioactive compounds will be subjected to anti-inflammatory targets using various modeling tools. Further, shortlisted bioactive compounds were subjected to *Invitro* analysis on cell based model system.

2. OBJECTIVES

1. Study on photochemical profiles of *Cassia auriculata linn* by *Insilico* approach.

2. Screening of bioactive compounds / phytochemicals by various methods for inflammatory activety.

3. *Insilico* validation studies of selective phytochemicals / bioactive compounds for various pharmacological parameters.

4. *Invitro* validation studies of selected/screened phytochemicals for Inflammation studies on cell based modal system.

3. Significance of study:

The study helps to identify important bioactive compounds for therapeutic use and also validate the traditional or ethnic use of cassia auriculata linn plant against inflammatory diseases.

4. Methodology

1. Plant extraction

The whole plant extraction of cassia occidentalis linn by cold maceration method for screening phytochemicals and phytoconstituents in plant. Collected plant is washed by tap water and separate parts of plant like leaves, flowers, stem, seeds and pods. Keep all plant materials to drying for 7-10 days in shad. Dried plant materials were thoroughly crushed using motor and pestle. 350g of dried pant powder of plant material was soaked in sequential preparation of extracts with solvents that are Hexane, Ethyl acetate, Methanol and Aqueous in brown bottle at 25℃ for three days and kept in a wooden cabinet. The mixture was shaken periodically and then filtered using cotton wool. The filtrate was poured in labeled kidney dishes of known weight and dried off in the oven at 50 for two days, leaving a dark green residue which was weighed and placed in a glass bottle and kept at 4 for further use. A stock solution of the extract was prepared immediately with distilled water before the start of the acute toxicity evaluation experiments. Extracted plant materials were taken to separate phytochemicals and bioactive compounds by LCMS.

2. Pro-inflammatory cytokines 3D structure identification

Identify the proinflammatory cytokines and the 3D structure identification of proinflammatory cytokines by using PDB database and chemical structure of natural compounds by using pubChem database or Schaech chemical structure using MarvinSketch/chemsketch. The CASTp server is using for active sites maping. Characterization and validating by using SAVES server (structure analysis and verification server).

3. Physicochemical and ADMET property prediction

The phytochemical compounds analyzing insilico for drug likeness. Predict ADMET property by using admetSAR tool. Toxicity checking by pro-tox II tool. The compounds are modified based on physical and chemical properties by using pharmacokinetic properties. It will be identified on the bases of Lipinski's Rule of Five. The quantitative structure activity relationship (QSAR) using for novel analogues rationally designed on the bases of structure activity relationship. The designed analogues were further analyzing insilico for drug-likeness.

4. Molecular docking and dynamic simulation

Molecular docking study will carry out by using Schrodinger suit (maestro) and further proceeded for insilico validation through molecular dynamic simulation to know the stability of protein and ligand complexity by using Desmond.

5. Invitro validation

Screened phytochemicals for inflammatory disease after docking and simulating process, those compounds are used for invitro analysis on cell based modal system.

Work plan

- **Bar diagram**

Activities	Year 1		Year 2		Year 3	
	1-6 Months	7-12 Months	13-18 Months	19-24 Months	25-30 Months	31-36 Months
Literature survey.						
Collected whole plant extraction by different solvents and separation compounds by LCMS.						
Identification of Pro-inflammatory cytokines 3D structure and active site prediction.						
Insilico study of characterization and validation of pro-inflammatory cytokines.						
Physicochemical and ADMET property prediction and quantitative structure activity relationship.						
Insilico molecular docking using Schrodinger suit (maestro) and dynamic simulation using Desmond						
Invitro analysis on cell based modal system						
Any unfinished work from previous period will be done. The manuscripts will be prepared for publication.						

1. References

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